## REMARKS

Applicants present claims 45-79 to the present invention regarding the growth factor, its method of separation and its medical use. These Claims 44-79 are general modifications of the claims as now examined and issued in the equivalent European application Serial No. 90907823.0 and in the copending U.S. Ser. No. 08/473,276 (for human VEGF factor).

Applicants present these pending claims. In particular, now only bovine factor or bovine DNA is claimed.

Claims 44-79 are presented as follows:

Claims 44 to 47 now claim only bovine growth factor.

Claims 48 to 53 claims only bovine factor.

Claim 54 claims only bovine factor.

Claim 55 claims a pharmaceutical composition of bovine cells.

Claims 56 and 57 claims only a method of wound healing with bovine growth factor.

Claims 58-60 claim a pharmaceutical composition for use in wound healing.

Claim 62 claims a treatment method for wounds using the factor.

Claim 63 claims a pharmaceutical composition.

Claims 64-65 claim only bovine growth factor.

Claims 66 and 67 claim only DNA for the bovine growth factor.

Claims 68 to 73 claim an in vivo method of wound healing using the bovine factor.

Claims 74 to 79 claims pharmaceutical composition claims are based on bovine factor.

In particular amended Claims 58, 59 and 60 now claim a pharmaceutical composition for a bovine factor for in vivo wound healing in a human. These claims are similar to the claims which will issue in our copending application U.S. Ser. No. 08/473,276, as U.S. Patent No. 6,899,882 on May 24, 2005.

Applicants have amended now the pending claims to further explain and define the present invention. Only bovine VEGF factor is claimed and its use as pharmaceutical composition in in vivo wound healing in a human is claimed.

No new matter is added to the application.

We turn now to the specific rejections.

The Examiner states:

"Claims 1-44 have been cancelled. Claims 45-79 are newly submitted. Any rejection not expressly maintained or presented herein has been withdrawn in view of applicants amendments to the claims.

The double patenting rejection over the claims of application 08/473276 is withdrawn, as the current claims are restricted to bovine VEGF, and the copending claims are restricted to human VEGF.

Newly introduced claims 61 and 64-68 are in a product-by-process format. The purification or production of a protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCP A 1972). Therefore, even if a particular process used to prepare a protein is novel and unobvious over the prior art, the protein per se, even when limited to the particular process, is unpatentable over the same protein taught by the prior art. See In re King, 107 F.2d 618, *620,* 43 u.S.P.Q. *400,* 402 (c.c.P.A. 1939); In re Merz, 97 F.2d 599, 601, 38 U.S.P.Q. 143, 144-45 (C.C.P.A. 1938); In re Bergy, 563 F.2d 1031, 1035, 195 U.S.P.Q. 344, 348 (c.C.P.A. 1977) vacated 438 U.S. 902 (1978); and United States v. CibaGeigy Corp., 508 F. Supp. 1157, 1171, 211 U.S.P.Q. 529, 543 (D.N.J. 1979). As none of the recited processes would result in a particular degree of purity, nor affect the composition of the resultant protein, such limitations are given only minimal weight in considering the prior art. With respect to issues under 35 U.S.C. §112, first paragraph, all claim limitations must be considered.

Claims 56, 57 and 68-73 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/29/2003.

Claims 74-79 are hybrid claims, being drawn to the pharmaceutical composition used in the method of the claims from which they depend. As such claims would not be properly dependent if interpreted to be composition claims, as a composition does not further limit a method (they are distinct categories of invention), the claims are interpreted as limiting the composition being used in the method. As such, they are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/29/2003.

Newly introduced claims 45-55 and 58-67 are under consideration."

## TERMINAL DISCLAIMER

"The terminal disclaimer filed on 8/23/2004 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 08/473276 has been reviewed and is accepted. The terminal disclaimer has been

recorded."

Applicants gratefully acknowledged this terminal disclaimer is accepted.

## OBJECTIONS TO THE SPECIFICATION

The Examiner states that:

"The disclosure is objected to because of the following infonnalities:
The amendment filed 8/23/2004 is objected to because it is not clear whether the statement that "the common text" of the parent applications is incorporated by reference refers to the text that the various parents have in common with each other, or that which each has in common with the instant application. If the fonner is the case, such would still be subject to a new matter rejection. If the latter is the case, the incorporation would not be improper, but would serve no purpose.
Appropriate correction is required."

Applicant has amended the text as requested for the parent applications of March 1989 and May 1989, in fact all disclosure of each was carried forward in the patent application which was filed in June 1989.

Reconsideration and withdrawal of this objection are respectfully requested.

## CLAIM OBJECTIONS

The Examiner states:

"Applicant is advised that should claims 45 and 47 be found allowable, claims 48 and 49, respectively, will be objected to under 37 CFR 1.75 as being substantial duplicates thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k)."

Applicants respectfully traverse this rejection.

Applicants argue these claims now have different limitations.

Reconsideration and withdrawal are respectfully requested.

## REJECTION OF CLAIMS 51, 55, 58-60, 62 AND 63 UNDER 35 USC 112

The Examiner states that:

"Claims 51, 55, 58-60, 62 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which
applicant regards as the invention.

Claim 51 is indefinite as it is not clear what is meant by '-.[1]'. Deletion of the period (".") would be remedial.

Claims 55, and 58 are indefinite for using the definite article 'the', rather than an indefinite article such as 'an' at the beginning of the claims. As there could be innumerable pharmaceutical compositions comprising the claimed protein, it is not clear to which one the article 'the' refers.

Claim 55 is also indefinite as it is not clear how the human being is being used. Further, it is not clear how the recitation of intended use further limits the pharmaceutical composition of claim 48. In this latter regard, claims 62 and 63 are similarly indefinite.

Claim 60 is indefinite because a pharmaceutical composition is not further limited by the dosage at which it is used, and because dosage is not an adaptation for wound healing.

The remaining claim(s) are rejected for depending from an indefinite claim.

Claims 64-67 are rejected under 35 US.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly introduced claims 64-67 are product-by-process claims requiring the recombinant expression of the claimed growth factor

The claims require the recombinant DNA production of the claimed protein. That would entail having the DNA encoding said protein, and expressing such in an appropriate host cell system. The nucleic acid sequences necessary for such recombinant production are not disclosed in the specification as originally filed. Vas-Cath Inc. v. Mahurkar, 19U5PQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Simply put, the claims require a full-length, functional nucleic acid sequence encoding folliculo-stellate derived growth factor, whereas the specification provides only a very small portion of the amino acid sequence of the bovine protein, and does not provide any nucleic acid sequence from any species. The specification merely provides an invitation to find the nucleic acid, and does not provide any evidence of possession of such nucleic acids. The skilled artisan cannot envision the detailed chemical structure of the polynucleotides required for the process recited in the rejected claims, and therefore conception is not achieved until reduction to practice has occurred, regardless

of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In this case only a partial amino acid sequence is provided. No complete amino acid sequence is provided, and no nucleic acids are provided.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115). Therefore, as the specification fails to describe the nucleic acids required to carry out the process recited in the claims, the claims fail to meet the written description provision of 35 u.S.c. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 u.S.c. §112 is severable from its enablement provision (see page 1115).

Applicants traversal that is would not require undue experimentation to obtain the required DNA has been fully considered but is not deemed persuasive. Such *might* be the case if the *entire* amino acid sequence of the protein had been disclosed. However, it has not. What is disclosed is a partial sequence, and an invitation to experiment. Such does not fulfill the written description requirement of 35 U.S.C. § 112, first paragraph. Applicant is again reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claims 64-67 19, 20 and 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record as applied to claims 19,20 and 40 in the previous Office Action.

Applicants traversal at page 16 of the response filed 8/18/2004 has been fully considered but is not deemed persuasive."

Applicants respectfully traverse this rejection.

In view of the newly presented claims, this rejection is overcome.

Reconsideration and withdrawal of the rejection are respectfully requested.

**REJECTION OF CLAIMS 64-67 UNDER 35 U.S.C. 112, FIRST PARAGRAPH**

Claims 64-67 are rejected under 35 U.S.C.112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner states:

"The claims read on folliculostellate derived growth factor from any source. Specification describes the protein only as isolated from human and bovine sources.

The Vas-Cath Inc. v. Mahurkar, 19U5PQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Calli at page 1116).

With the exception of the human and bovine proteins referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The protein itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. Although those cases related to the isolation of nucleic acids, the point is relevant here; although it would be reasonably predictable that other animal species would have homologous proteins, applicants have not evidenced either conception of such proteins, nor that they were in possession of such.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In this case the specification provides the bovine and human proteins and partial descriptions of each, but seeks cover for any and all proteins that might be termed "Folliculo stellate-derived growth factor", regardless of source.

Therefore, only human and bovine folliculo stellate-derived growth factors, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §§ 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §§112 is severable from its enablement provision (see page 1115)."

Applicants respectfully travers this rejection.

The arguments above are incorporated by reference.

Applicants argue that with the newly presented claims this rejection has been overcome.

Reconsideration and withdrawal are requested.

## REJECTION OF CLAIMS 45-55 and 58-67 UNDER 35 U.S.C. §§102 AND 103

Claims 45-55 and 58-67 are rejected under 35 U.S.C. §§ 102(e) as being anticipated by Connelly et al. (U.S. Pat. No. 5,008,196, cited by Applicants).

The Examiner states that:

"The reference teaches a vascular permeability growth factor, isolated from guinea pig cells, which is a disulfide linked dimer which is approximately 43 kDal on non-reduced SDS PAGE, which stimulates endothelial cell proliferation and is effective in would healing between 10-500 pg/ml. Connolly et al. teaches purification and characterization of an endothelial cell growth factor (col. 2,line 1 to col. 3, line 55), which is effective in would healing at 10pg/ml (half-maximal - see column 9, lines 57-61). Claims 14 and 18-20 recite FSdGF made by recombinant techniques and claims 29-30 and 34 35 recite FSdGF isolated via protein purification. Since the invention defined in a product-by-process claim is a product, not a process, then it is patentability of the product claimed and NOT of the recited process steps which must be established. Since the growth factor taught by Connolly reasonably appears to be the same as that of the instant application in terms of its molecular weight and activity even though it is derived from a different tissue source, the growth factor taught by Connolly appears to anticipate the protein of the instant application, absent evidence to the contrary."

Applicant respectfully traverse this rejection.

Applicants argue that the bovine claims are distinguished from guinea pig cell.

Therefore this rejection is overcome.

Reconsideration and withdrawal are respectfully requested.

## JOINT INVENTORSHIP / CLAIM REJECTIONS - 35 USC §§ 103

The Examiner states:

"This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §§ 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. §§ 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the

examiner to consider the applicability of potential 35 U.S.C. §§ 102(f) or (g) prior art under 35 U.S.C. §§ 103."

Applicants will examine this inventorship when claims are allowed.

## REJECTION OF CLAIMS 45-55 AND 58-67 UNDER 35 U.S.C. 103

Claims 45-55 AND 58-67 are rejected under 35 U.S.C. §§ 103 as being unpatentable over Connolly et al. (US. Pat. No. 5,008,196, cited by applicants) or Senger (Science, 219, 983-985, 1983, cited by applicants) or Dvorak (U.S. Pat. No. 4,456,550, cited by applicants) or Criscuolo et al (1. Neurosurg. 69, 254-262, 1988, cited by applicants), anyone of the aforementioned in view of Chen et al. (U.S. Pat. No. 5,073,492, cited by applicants) for reasons of record as applied to Claims 1-3, 11, 14-16, 18-25, 29-32, 34-37 and 40 in the previous office action.

The Examiner states:

> "The teachings of the primary references are discussed above. Each teaches isolation of VEGF from one or more animal species. However, none discloses bovine VEGF. '492 teaches the partial purification of bovine VEGF approximately the same size as guinea pig VPF (VEGF; Fig. 2, :traction III) which selectively stimulates endothelial cell growth (Fig. 5 and col. 4, line 6 to col. 5, line 6). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use the method of anyone of the primary references to purify bovine VEGF because '492 discloses that VEGF is present in bovine tissues. One would have been motivated to make this modification in order to have bovine VEGF for use in veterinary applications for cattle. Accordingly, the invention, taken as a whole, is *prima facie* obvious over the prior art."

The Examiner further states:

> "Applicants traversal that the rejection is overcome by the newly presented claims is not persuasive."

Applicants respectfully traverse this rejection.
Applicants now argue this rejection is overcome based on the newly amended claims.
Reconsideration and withdrawal are respectfully requested.

## PROVISIONAL DOUBLE PATENTING

The Examiner states that:

"The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman,* 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Long*759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 45-55 AND 58-63 are provisionally rejected
under the judicially created doctrine of double patenting over claims 26-35, 57, 66-68, 84, 89 and 90 of copending Application No. 10/177485. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.
The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: both applications are directed to folliculo stellate-derived growth factor in isolated fonn, and as this case is a continuation of 08/473276, the disclosures are identical.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller,* 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP §§ 804."

Applicants respectfully traverse this rejection.

Applicants are not the assignees of U.S. Ser. No. 10/177,485.

Applicants continue to seek cooperation with the assignees of U.S. Ser. No. 10/117,485.

Thus far no agreement has been reached.

Reconsideration and withdrawal are requested.

## DIFFERENT PROVISIONAL DOUBLE PATENTING

The Examiner states:

"Claims 45-55 and 58-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26-35 of copending Application No. 10/115492. Although the conflicting claims are not identical, they are not patentably distinct from each other because each is drawn to VEGF, including bovine VEGF, and compositions thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented."

"Claims 45-55 and 58-67 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending Application No. 10/177485 which has a common inventor with the instant application.

Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if published or patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future publication or patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective u.S. filing date of the copending application under 37 CFR 1.131. For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(1)(1) and § 706.02(1)(2).

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention 'by another,'or by a showing of a date of invention for the instant application prior to the effective V.S. filing date of the copending application under 37 CFR 1.131. For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP §§ 706.02(1)(1) and §§706.02(1)(2).

Claims 45-55 and 58-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 32-35 and 41 of copending Application No.1 0/155492. Although the conflicting claims are not identical, they are not patentably distinct from each other because each is drawn to VEGF, including bovine VEGF, and compositions thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting
claims have not in fact been patented.

Claims 45-55 and 58-67 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending Application No.1 0/155492 which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if

published or patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future publication or patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective US. filing date of the copending application under 37 CFR 1.131. For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(1)(1) and §706.02(1)(2).

Applicants respectfully traverse this rejection.

Applicants are pursuing a Declaration regarding this aspect of the invention.

Applicants continue to seek cooperation with the assignees of U.S. Ser. No. 10/117,485.

Thus far these has been no agreement reached.

Reconsideration and withdrawal are requested based on the newly presented claims.

## CONCLUSION

It is believed that the present Amendments place the application in condition for allowance. Allowance of claims 45-79 is respectfully requested. Such action, as well as the timely issuance of a Notice of Allowance is earnestly solicited. If a telephone conference would be useful in this case, the Examiner is encouraged to call the undersigned at the number below to discuss any prosecution issues.

Respectfully submitted,

PETERS, VERNY, JONES, SCHMITT & ASTON, LLP

Date: May 23, 2005

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Enclosure: Combined Petition for Extension of Time and Notice of Appeal and Fee